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# Special Populations and Considerations in Migraine Therapy

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# Special Populations and Considerations in Migraine Therapy

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# Comorbidity

- Comorbid – Occurrence of two medical disorders in the same individual at a frequency greater than chance
  
- Most noted Migraine Comorbidities
  - Depression / Anxiety
  - Cardiovascular
  - Fibromyalgia
  - Seizures

# Migraine Comorbidities

- Psychiatric
- Neurological
- GI
- Cardiovascular
- Allergy / Immunity

# Migraine Comorbidities

- Psychiatric
  - Depression
  - Anxiety
  - Panic Attacks
  - Bipolar Disorder
  - Obsessive Compulsive Disorder
  - Phobia Disorder

# Migraine Comorbidities

■ Psychiatric	Odds Ratio
— Depression	2.2-3.4
— Anxiety	2.7
— Panic Attacks	3-5.1
— Bipolar Disorder	2.9-7.3
— Obsessive Compulsive Disorder	
— Phobia Disorder	3.4

# Migraine Comorbidities

## ■ Depression

Major Depression increases risk of  
Migraines



Migraines increase risk of Major  
Depression

# Migraine Comorbidities

- Cardiovascular
  - Patent Foramen Ovale
    - 30-40% Migraine with Aura
  - Atrial Septal Aneurysm
    - 28.5% Migraine with Aura
  - Mitral Valve Prolapse
  - Hypotension
  - Hypercoagulable State



# Prevalence of PFO and Migraine

## (Literature)

	Migraine	No Migraine
Del Sette	41%	16%
Anzola	48%	20%
Schwerzmann	47%	17%
Domitrz	54%	25%

# Migraines and PFO Closure

- Some small case series showed improvement with closure
  - Schwerzmann 2004
    - 54 % (M+) – 62 % (M-) decrease
  - Post et al 2004
    - 50 % (M-) – 71 % (M+) decrease

M- = Migraine without Aura

M+ = Migraine with Aura

# Migraine and Vascular

## ■ Cardiovascular

### — Women's Health Study

- Migraine with Aura

2X likely to have stroke / cardiovascular disease

### — Physicians Health Study (men)

- Increased risk of MI
- Increased risk of Cardiovascular Disease

# American Migraine Study

## ■ Risk Stroke

■ Migraine	1.54
■ M with Aura	2.78
■ M without Aura	0.97

## ■ Cardiovasc

■ Migraine	2.16
■ M with Aura	2.86
■ M without Aura	1.85

# Migraine and Vascular

- Endothelial Dysfunction
  - Elevated Prothrombin levels
    - Migraine with Aura
  - Elevated Von Willebrand Factor  
(Procoagulant promoting platelet adherence)
  - Hypercoagulable State

# Migraine Comorbidities

## ■ Sleep Disorders

- More lifetime sleep problems in Migraine patients
  - Inadequate sleep
  - Difficulty initiating sleep
  - Persistent nightmares
- Case Series (3582 patients)
  - ½ patients with onset of migraine between 4am and 9am

# Migraine Comorbidities

- Gastrointestinal
  - Irritable Bowel Syndrome
  - Gastritis
  - Peptic Ulcer Disease
  - GERD
  - Colitis

# Migraine Comorbidities

## Neurological

- Vertigo
- Motion Sickness
- Essential Tremor
- Stroke
- Epilepsy
- Autonomic Nervous System
- Fibromyalgia
- Restless Leg Syndrome



# Migraine Comorbidities

- Migraine – Associated Vertigo
  - Dizziness clinic
    - 38% had migraine diagnosis
  - Migraine clinic
    - 9% suffered vertigo  
(0.5% suffer vertigo in control population)

# Migraine Comorbidities

- **Migraine – Associated Vertigo**
  - Difficult to associate as onset of Migraines precedes Vertigo by years...
    - Migraines – early 20's
    - Vertigo – 30s – 40s
  - Population Studies
    - Approx. 5% report consistent migraine and vertigo
    - Up to 70% report some combined episodes
    - Up to 30 % vertigo without migraine

# Migraine Comorbidities

## Migrainous Vertigo Criteria

### ■ Definite

- Episodic Vestibular symptoms of at least moderate severity
- IHS Migraine Diagnosis
- At least 1 of the following migrainous symptoms during at least 2 vertigo attacks
  - Headache, Photophobia, Phonophobia, Aura

### ■ Probable

- Episodic Vestibular symptoms of at least moderate severity
- At least 1 of the following
  - Migraines
  - Migraine like triggers for vertigo
  - Migraine symptoms during vertigo
    - Photophobia, Phonophobia, Visual aura

# Migraine Comorbidities

## Autonomic Symptoms

- Orthostatic Intolerance
  - Migraine – 39.1%    Control – 5.6%
- Syncopy
  - Migraine – 46%    Control – 31%
- Postural Orthostatic Tachycardic Syndrome (POTS)

# Migraine Comorbidities

- Postural Orthostatic Tachycardia Syndrome
  - Heart rate increase  $\geq 30$  beats per minute with standing 5 – 10 minutes
  - Symptoms occur with standing, resolve with lying
    - Leg Mottling with standing
  - Women 4-5X more common
  - Co-morbidities
    - IBS, joint hypermobility

# Migraine Comorbidities

- POTS and Migraines
  - Small Case Series
    - 1 in 5 migraines associated with POTS
  - Tilt Table induced symptoms in 16 minutes
  - Normal Work up
    - MRI, EEG

# Migraine Comorbidities

- Fibromyalgia
  - Prevalence – 2% in North America
  - Women affected *3 times more* than men
  - Peak Age
    - 55 – 64 years old

# Migraine Comorbidities

- Prevalence of Migraine in Fibromyalgia  
Case Series; Clinical Rheum journal 2005
  - Headache occurred in up to 76% patients
  - Migraine was seen in 48% patients
  
- Prevalence of Fibromyalgia in Migraneurs  
Cephalgia 2006
  - 17% in episodic migraine
  - 35% in chronic migraine

(FBM prevalence = 2% in normal population)



# Migraine Comorbidities

## ■ Fibromyalgia

- Cymbalta approval for Fibromyalgia
  - Physical Exercise + Cymbalta = most effective
  - Physical Exercise = second
  - Cymbalta = significant

# Migraine Comorbidities

- Complex Regional Pain Syndrome
  - 3.6 times more likely to be migraine sufferers
  - 2 times more likely to suffer Chronic Daily headaches
- If history of migraines
  - Earlier onset of CRPS
  - Involves more limbs

# “Migralepsy”

- Migraine and Epilepsy
  - Multiple studies indicate comorbid disease
    - Prevalance of Seizures
      - Migraine sufferers – Up to 17%
      - Non Migraine – 0.5 - 0.8%
    - Headache very common *after* seizure during post-ictal state

# “Migralepsy”

- IHS criteria
  - i) Migraine with aura
  - ii) Seizure with or within 1 hour after migraine with aura attack
  
- Hypothesis / Pathophysiology
  - Cortical suppression by aura
  - Occipital cortex of Migraineurs with lowered excitation threshold (resistance)

# Migraine Comorbidities

## ■ Allergies

- Asthma, Hay Fever, Chronic Allergic Rhinitis – seen more often

## ■ IgG food allergy testing

- Screen for food allergy
- Check levels of IgG with foods
- Avoid foods which result in increased IgG

## Women and Migraines

- Peak of migraine frequency during days -3 and +2 of the start of menstrual flow.
- 60% of women
  - have an increase risk of migraines during the premenstrual phase of decreasing estrogen levels.

# Hypothesis

- Estrogen modulates inhibitory peptide function in the trigeminal nerve.
  - When estrogen levels fall, the downregulating effect on inflammatory genes is removed.
- Compensatory mechanisms cannot always be invoked quickly enough to avoid headache.
- Is not seen with low E2 states maintained for months or years
  - Is seen with fluctuating E2 levels and irregular bleeding

# Conclusion

- Comorbidities are common and well recognized
- Treatment of the comorbidities may help prevent...
  - Vertigo attacks triggering Migraines
  - Allergies
- Basis of choosing preventative therapy is to attempt to treat Comorbidities
  - Insomnia = Nortriptyline
  - Anxiety = Depakote or Cymbalta